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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

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8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/070,439	MURAKAMI ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears n the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5&7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to an application filed on 5/30/02. There are six claims pending and six under consideration. Claims 5 and 6 appear to be compound claims. Claims 1-4 are use claims. This is the first action on the merits. The application concerns some fatty acid esters of the compound Coenzyme A compounds, compositions, and uses thereof. The Examiner is interpreting Applicants' claim limitation "fatty acid CoA thioester" to mean compounds derived from acetyl coenzyme A by replacement of the acetate group on sulfur by fatty acids. Eric Weisstein's World of Science defines fatty acid as a "long chain monocarboxylic acid containing an even number of carbon atoms".

Title

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: inserting the phrase "Fatty Acid CoA Thioester" at the beginning of the title.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Claims 1-4 provides for the application of fatty acid CoA thioester compounds, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-4 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

4. If claims 5 and 6 are intended to be composition claims, then they are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential element. See MPEP § 2172.01. The omitted element is: the carrier required to make a composition. Without a carrier, the claim is just a compound claim.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating diabetes or obesity. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

a) Determining if any particular claimed compound would treat diabetes or obesity would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large degree of experimentation. b) The direction concerning treating diabetes or obesity is found in the passage spanning paragraph 1, page 5 to paragraph 1, page 6, which merely

states Applicants' intention to do so. Applicants describe no formulations or doses required to practice. Applicants describe their compounds as inhibitors (antagonists) of the PPAR receptors. Since no PPAR antagonist has ever been used to treat any human disease, how is the skilled physician to know what dose to use for each of these two different diseases? There is a *in vitro* assay for receptor binding described in the passage spanning paragraph 4, page 6 to paragraph 1, page 9 with data for six compounds. It is unclear if this assay is correlated to diabetes or obesity treatment. c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease with PPARα or PPARγ receptor antagonists, which involves physiological activity.

e) The state of the clinical arts in PPARα or PPARγ diseases is reported by Nuss (Ann. Reports Med. Chem.). In the first complete paragraph on page 215, the reference reports that agonists of the PPARγ receptor lower blood glucose. The thiazolidedione compounds troglitazone, rosiglitazone, and pioglitazone are PPARγ agonists used to treat diabetes. These three compounds are structurally unrelated to those of Applicants. Agonists have the opposite biological effect of that of Applicants' antagonists. Applicants' antagonists, would of course exacerbate, the diabetic conditions that Applicants intended to treat. As shown on page 463 of Kane (Biochemistry) fatty acid CoA thioester compounds are

necessary intermediates in the synthesis of fats in the cytosol of cells. Would not administration of fatty acid CoA thioester compounds to a fat Patent Examiner simply make that person fatter?

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The scope of the claims involves the dozens of compounds embraced by the term "fatty acid CoA thioester" and treatment of two diseases. Thus, the scope of claims is narrow.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Nordlie (Journal of Biological Chemistry). The reference teaches both inhibition and stimulation of glucose-6-phosphate and phosphohydrolase and pyrophosphate-glucose phosphotransferase with palmitoyl CoA. The finding is located in the paragraph spanning lines 4144-4145 and in Fig. on page 4145. The implication of this for diabetes treatment is found in the final sentence of the abstract and in the first sentence of the second complete paragraph on page 4148 of the reference. Thus, if this is a method of treatment claim, then it is anticipated by this reference. The solution of palmitoyl CoA in cacodylate buffer is a composition. Thus, if claim 5 is a composition claim, then it is anticipated by these references.

7. Claims 5 and 6 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention. Fatty acid CoA thioester compounds are naturally occurring substances. The phrase "therapeutic agent for the ketoacidosis" is a statement of intent and places no additional physical limitations upon the claims. The word "containing" is an open term and includes the compounds alone. Thus, claims 5 and 6 read upon the pure compounds. Sigma Chemical Company offered twenty-four such compounds for sale.

Allowable Subject Matter

8. Claims 1-4 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action. The following is a statement of reasons for the indication of allowable subject

matter: There are no therapeutic implications associated with claims 1-4, just inhibition of the receptor sites. While Hertz (Nature) showed that "fatty acid CoA thioester" compounds bind to the nuclear receptor HNF-4α in 1998. The earliest t published report of antagonism at the PPAR sites is Elholm (J. Biological Chem.). This reference is dated in 2001 and is not a competent reference against Applicants' claims because of the publication date.

Conclusion

9. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK